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RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS

AND INTERFERENCES

Ex Parte JOHN C. BELL, NAHUM SONENBERG, DAVID F. STOJDL, EARL G. BROWN, HAROLD L. ATKINS, *and* RICARDO M. MARIUS

Appeal 2010-004413
Application 09/664,444
Technology Center 1600

Oral Hearing Held: May 12, 2009

Before ERIC B. GRIMES, FRANCISCO C. PRATS, and JEFFREY N. FREDMAN, *Administrative Patent Judges.*

APPEARANCES:

ON BEHALF OF THE APPELLANT:

DOUGLAS A. GOLIGHTLY, ESQUIRE
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The above-entitled matter came on for hearing on Thursday, May 12, 2011, commencing at 9:40 p.m., at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia, before John Hutson.

P R O C E E D I N G S

THE USHER: Calendar No. 40, Appeal No. 2010-4413. Mr. Golightly.

JUDGE GRIMES: Good morning, Mr. Golightly. You'll have 20 minutes to make your argument and you can get started whenever you're ready. If you wouldn't mind introducing your colleague for the record, we'd appreciate it.

MR. GOLIGHTLY: Sure. My name's Doug Golightly, and my colleague is Asaf Batleman (ph). We work at the same company.

So I think the Rejections comes down to they are related to lack of enablement and there's two main Rejections. One Rejection relates to Dependent Claims 27, 31, and 73 to 77, which just recite specific VSB strains. The Examiner alleges that a biological deposit for the enablement of these claims. Our arguments on the record, we believe, will over come the Rejections, and we'll discuss that Rejection today only as time allows.

So what we want to focus on is the Rejection that the claims lack enablement with respect to methods involving immunocompetent animals and treatments. With the exception of Claim 78 which is limited to in vitro, all the dependent claims are presented -- are presently rejected under 35 U.S.C., 112, first paragraph, because allegedly the Specification, while being enabling for methods utilizing VSP for reducing the viability of -- tumor

cells in vitro and are enabling for in vivo and xenographs, they do not reasonably provide enablement for utilization of VSV for the reduction of viability of all types of -- tumor cells in an immunocompetent animal. That's the Examiner's position.

As I will discuss, this Rejection focuses on really three allegations: One, the Claims are enabled for in vivo treatment of an immunocompetent animal; the rejected claims specifically relate to treatment; and, third, the application fails to enable the genus -- tumor cells.

JUDGE FREDMAN: The Examiner actually doesn't have any specific reference. In fact, this is a suggestion -- number of references that are commonly used in enablement rejections, like Jane Freshley (ph) and Germ Rangora (ph), and basically alleges that there's unpredictability, which certainly there is, but has no specific unpredictability with regard to your oncolytic virus.

MR. GOLIGHTLY: Yes, that's one of my paragraphs I was going to go over, yeah. Yeah, I mean, I agree. I don't think it's specific and I'll talk about that later. I don't think it's really relevant to the claims as they're drafted and they're not particularly relevant to our VSV claims.

Not to jump too far ahead of what I planned to say, but we did cite some references. We cited to McCormick and Cora (ph) which are some oncolytic virus references out there, and we cited them just to show that those authors/inventors used in vitro studies, xenographs, and those did predict the clinical results they saw. The Examiner dismissed that and said those don't relate to VSV so, therefore, I'm not giving them any weight, is essentially what he said. But based on that argument, the references you

cited also don't have the relevance. So I think ours were more relevant, and he dismissed those.

So I guess what I first talked about is the claims do not specifically relate to therapy and to treatment, and I cited -- they refer to reducing viability of a tumor cell. The Examiner has alleged that this is pre se treatment and then concludes that the claimed invention is not enabled for treating an immunocompetent animal. However, the rejected claims do not specifically recite treatment, so we believe the Examiner is applying the wrong standard.

JUDGE FREDMAN: I do have one question about that, though. In the context of an immunocompetent animal, wouldn't the virus function -- I mean, I don't know that this is necessarily relevant to the enablement, as you say, because the claim doesn't necessarily encompass this, but wouldn't the VSV virus presumably stimulate an immune response which would then reduce the ability of the virus to target the tumor cells in an immunocompetent animal?

MR. GOLIGHTLY: So the Examiner hasn't made that argument. Also, we haven't addressed that here. I don't want to get into too much detail because I haven't really prepared for it. I'd have to confer with the inventors, but there are obviously differences between immunocompetent and immunodeficient. However, we believe that there were techniques and methods available and under those skilled in the art at the time of the invention that would have allowed them to reduce the viability of those tumor cells. Even in spite of that -- I mean, you can think of simply directly injecting the tumor. There are ways to knock down that immune response.

JUDGE FREDMAN: Well, I think there are multiple strains of VSV, so you could also use different strains sequentially.

MR. GOLIGHTLY: Yes. And VSV is -- I don't want to venture too far -- but I don't think it's --

JUDGE FREDMAN: It's not particularly --

MR. GOLIGHTLY: Well, and it's not a particular human pathogen, so some people don't -- it's not like not some of the adenoval (ph) vectors and stuff.

And just so we're clear, our position is that even if the claims did explicitly recite treating immunocompetent animal, the Specification does enable that embodiment, also, and I'll discuss that a little bit later.

In our Reply Brief, we cited three different nonprecedential decisions from the Board to support our position. The first was *Ex Parte Booten* (ph). It has some significant similarities to the present situation. In that case, the Examiner's position was that the claims related to methods of transferring a neoclaic (ph) acid to cells that were enabled for in vitro transfer but not for in vivo transfer because the only purpose in the application, alleged by the Examiner, was in vivo transfer for therapy, and the claims would not have been enabled for these therapeutic purposes. Applicants in that case argued that the claims do not require therapeutic effect and that the application did demonstrate in vivo neoclaic acid transfer.

The Board essentially said in the decision that even if one were to accept the gene therapy -- or accept that gene therapy would've required undue experimentation and that gene therapy is the only in vivo use, the Board still not agree that the claims were not enabled. There was no reason to doubt that the in vivo neoclaic acid transfer would require undue

experimentation, even if therapeutic results might require undue experimentation.

The Board stated, and I quote, "When the claims are not directed to a method that achieves a therapeutically useful result, achieving such a result is not required for the claims to be enabled." They go on to say "Thus, while the claims read on gene therapy methods, they do not require producing a clinically effective therapeutic response."

Like *Booten*, the pending claims do not require any therapeutic effect, and the Examiner incorrectly considers the methods performed in vitro to be enabled but not for a therapeutic effect in vitro.

One of the other cases was *Ex Parte Sato Zao* (ph). The claims at issue were to methods to introduce neoclaic acid to molecules in -- subject. The Examiner rejected them as not being enabled essentially due to the alleged art recognized to unpredictability of achieving therapeutic levels following administration in vivo. The Board decided that the claims were enabled essentially because the Examiner's reasoning was not entirely consistent with the case law which says that enabling the full claim scope does not necessarily require enabling every embodiment and that the claims were not nonenabled. The Board even stated that, and I quote, "The Examiner may be correct that achieving clinically useful gene therapy using the claimed method would require undue experimentation, but the claims are not enabled merely for encompassing that difficult to achieve outcome." For clarity, the Examiner in the present case has not even shown that achieving a therapeutic effect using the claimed invention would require undue experimentation.

And then the last case I cited was *Ex Parte Iesi* (ph), and it's another similar decision. It recited a method that may encompass methods capable of achieving a clinically effective therapeutic response. Again the Examiner focused on the therapeutic effect and again the Board decided that while there may be potential problems and may complicate treatment, these problems need not be overcome for the enablement of the claims.

In the present application, the Examiner responded to applicants' discussion of these decisions by stating that "Contrary to applicants' assertion, the reduction in the viability of a tumor cell in the context of a living being constitutes a therapeutic response," and that was really the only argument we saw from the Examiner trying to rebut what these cases say. Therefore, in the present case, the Examiner's enablement analysis improperly focuses on whether the subject matter of the pending claims is enabled for methods that result in a therapeutic effect. Additionally, even if the claims required a therapeutic effect, they would meet the enablement requirement.

So the question is what is the correct level at which the present claims must be enabled? The real requirement that the claims must be enabled for reducing the viability of a tumor cell. The Examiner has not provided any valid reason that one skilled in the art at the time of the invention would have doubted the claimed invention would result in a reduction in viability, either in vitro, in vivo, even in an immunocompetent animal. It's not really on the record. The Specification shows that VSV clearly reduces the viability of tumor cells in vivo in the xenograph model, and there's been no evidence provided that suggests otherwise.

If a virus that has been extensively shown in our Specification to kill cells in vitro and in the mouse model, then its administration or delivery to a tumor cell in an immunocompetent animal would also be expected to result in reduction of viability, without requiring undue experimentation and using only skills that were known in the art at the time of the invention. The Examiner has really presented nothing to refute this.

So then the Examiner in making these rejections has gone on to cite many documents, which you brought up, and really they merely just point out that not all agents that have had activity in xenographs make it through clinical trials to become drugs. Many of these agents are dropped as drug candidates, not because they didn't have activity, the predicted activity, but because of side effects; they may have exhibited activity but not enough for the standard of care that was out there. However, the present claims only require activity, not approval by the FDA and not commercial development.

The cited claims, as a whole, do not stand for the proposition that activity seen in a xenograph will not be seen in an immunocompetent animal or in a patient.

JUDGE FREDMAN: I think we understand that. Can we jump to the other Rejection, which I think I had a couple questions on?

MR. GOLIGHTLY: Okay.

JUDGE FREDMAN: Essentially, we're talking about the deposit of these five strains, and I guess you're saying that they're found in several references and rely on the journal policy. You know, journal policies may say something, but that doesn't mean that's what people actually do. Certainly, they're not as available as if they were deposited at ATCC under the -- but the first question I have is, so you have a lot of sequence in this

case. Do you have the complete sequence of these viruses or just almost the complete sequence?

MR. GOLIGHTLY: Looking at the Specification, we have the sequence of the cDNAs for the proteins of the virus.

JUDGE FREDMAN: So you don't have all the upstream and downstream regulatory sequences?

MR. GOLIGHTLY: I do not believe we have the untranslated version.

JUDGE FREDMAN: So someone could recreate most of the viruses, I mean, nowadays but not --

MR. GOLIGHTLY: Yes, and I think looking back in the literature, they might -- I don't want to venture in to where I don't know, but --

JUDGE FREDMAN: I'm pretty sure the sequence of VSV -- some strains is disclosed, that's what you're getting at?

,MR. GOLIGHTLY: Yes, and I think some of them even -- they know what the parental strain is, so those sequences should be available.

JUDGE FREDMAN: And then four of the strains you have papers for. The fifth strain, I guess, is really strain 4, I think, M-4 strain, seems like there were no papers on. Is that strain -- I mean, you argue they're readily available, but who is it readily available from?

MR. GOLIGHTLY: I'm not sure.

JUDGE FREDMAN: I mean, that issue is a little bit concerning to me. Obviously, to some extent, this is the validity of the patent of those claims. I mean, not the whole patent, but it would be -- those claims would be subject to invalidity if it wasn't available. So there's an advantage here in depositing that may not, you know -- it may not, you know, actually

disadvantage you. I mean, here the immunoreaction would be in your favor, so -- asking you to do this.

MR. GOLIGHTLY: Okay. I think the one thing to respond is that what is the level that they have to be available? They're clearly out there, clearly lots of people and they are using an exchange --

JUDGE FREDMAN: Right. For M-1, 3, and 5 it's clear that they're published in a number of papers, so those ones seem more available. They don't meet the standard, we can argue, but they're more available. And 4, it seems like there might be more of an issue.

MR. GOLIGHTLY: Yeah, and I think I argued them for --

JUDGE PRATS: You argued M-4 separately and you said that the sequence -- that you would basically provide a sequence for all the viral proteins. So not to put words in your mouth, but are you essentially saying since the overall sequence of VSV is known, since we've given you the importance sequences with respect to strain 4, then you would basically be able to make it? That seems to be what the Examiner is sort of responding to, that statement. Is that accurate?

MR. GOLIGHTLY: What's the question?

JUDGE PRATS: That you'd be able to make it based on -- you're arguing that you'd be able to make it based on what's disclosed in the Specification.

JUDGE FREDMAN: Why would you be able to do that?

MR. GOLIGHTLY: I'd have to look more into that to see what -- exactly where that strain come from, what the background is, and whether other information's available.

JUDGE PRATS: Thank you.

JUDGE GRIMES: Thank you very much.

MR. GOLIGHTLY: Thank you.

(Whereupon, the proceedings, at 9:55 a.m., were concluded.)